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CPT-11 in the treatment of colorectal cancer: clinical efficacy and safety profile.

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CPT-11 (irinotecan) is a promising anticancer agent with a novel mechanism of action dependent on the inhibition of the DNA eukaryotic enzyme, topoisomerase I. The clinical utility of CPT-11 in advanced colorectal cancer has been documented in more than 400 patients recruited in phase II clinical trials in Europe, Japan, and United States. Among 178 eligible patients in a multicenter European study, the overall response rate to CPT-11 on a once-every-3-weeks regimen was 18%, and the median duration of response was 9.1 months. Thirty-two percent of the patients had no evidence of disease progression at 6 months. These results were similar in chemotherapy-naive and pretreated patients. These findings are consistent with the results of other studies conducted in Japan and the United States in which a weekly CPT-11 regimen was associated with response rates of 15% to 32% in chemotherapy-naive or pretreated patients. The principal adverse events of CPT-11 are neutropenia and delayed diarrhea, which in the European studies developed as grade 3 or 4 toxicity in 21% and 12% of the cycles (47% and 38% of patients), respectively. Neutropenia did not appear to be cumulative, with total recovery by day 22 in most cases. Loperamide was considered the most effective agent for controlling delayed diarrhea. Other adverse events included an early cholinergic-like syndrome (consisting of diaphoresis, early diarrhea, and abdominal cramps), nausea and vomiting, fatigue, and alopecia. In conclusion, CPT-11 has shown promising antitumor activity in the treatment of patients with advanced colorectal cancer, including those refractory to 5-fluorouracil (5-FU)-based regimens, suggesting no cross-resistance to 5-FU. CPT-11 appears to have activity similar to that of 5-FU in first-line treatment and, moreover, remains active after failure of 5-FU therapy. The specific gastrointestinal toxicity is

manageable, and a better control of this type of toxicity is expected in the future. CPT-11 would therefore appear a welcome addition to the oncology armamentarium for this difficult-to-treat malignancy.

Publication Types:
- Review
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